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Medical College

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Markus W. Reidenberg, M.D., F.A.C.P.
Professor of Pharmacology and Medicine
Chief, Division of Clinical Pharmacology
1300 York Avenue, Box 70
New York, NY 10021

Department of Pharmacology
Department of Medicine
Division of Clinical Pharmacology

Tel: 212 746-6227
Fax: 212 746-8835
E-mail: mmreid@mail.med.
cornell.edu

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Dockets Management Branch (HFA 305)
Food and Drug Administration
5630 Fishers Lane, room 1061
Rockville, MD 20852

Dear Sir:

We are submitting these comments for the Over-The-Counter Drug Products Hearing under item II B, Classes of Products, to request consideration of making some inhaled adrenal corticosteroid formulations and inhaled cromolyn available over-the-counter (OTC), so that asthmatic patients will be able to purchase them to maintain continuous chronic therapy without the need to obtain periodic prescriptions to continue their treatment.

The prevalence and severity of asthma is very high among poor and homeless children in New York. A funded survey conducted in homeless shelters in New York City found that 40% to 50% of children have moderate to severe asthma as compared to 6% to 10% of the general population of school children (McLean). Consequently, emphasis must be placed on effective measures that will improve management of the disease and the well being of the asthma sufferer. As many as 80% of these children with asthma present with symptoms before the age of five. When surveyed, a substantial fraction of their parents reported that they are aware of their child's diagnosis but do not provide treatment due to lack of a prescription (McLean). Therefore, by making inhaled corticosteroids available OTC, the barrier of requiring a prescription to get adequate treatment will be eliminated.

Early intervention with inhaled corticosteroids is considered an essential component of first line treatment of persistent asthma (White, 1999). Inhaled corticosteroids have been shown to provide long term preservation of pulmonary

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function and may prevent irreversible airway obstruction, airway remodeling, and hyperresponsiveness. There is still reluctance by some to use these drugs despite their being the present standard of care because of an exaggerated fear of side effects. The most commonly recognized adverse effects are oral irritation and candidiasis and dysphonia. These local effects cause no significant morbidity and are not improved with required routine visits to a physician just to get a prescription for inhaled corticosteroids. In addition, very rare cases of hypersensitivity reactions have been reported, which warrant an immediate evaluation by a physician and not waiting for a scheduled visit.

Systemic effects of inhaled corticosteroids are rare, but two potentially serious adverse effects in children are hypothalamic-pituitary-adrenal (HPA) suppression and bone growth retardation. A double-blind, randomized study conducted by Wolthers and Pedersen investigating the linear growth of 43 school children with mild asthma treated with inhaled budesonide at 200, 400 and 800 ug/day for 12 weeks found significant growth suppression only with the budesonide dose of 800 ug/day (1992). The researchers concluded that inhaled budesonide can be safely used in doses up to 400 ug/day in school children with asthma. Thus, a safe OTC dose can be determined. We are not suggesting the use of this specific inhaled corticosteroid, but that inhaled corticosteroids as a class be considered and appropriate formulations be made available OTC with appropriate dosage directions for use. Again, it is not likely that routine office visits for the purpose of prescription renewal will alter the frequency of this adverse effect.

It is well documented that children given inhaled corticosteroids at therapeutic doses do not have adrenal suppression. The effects on adrenal function of high dose inhaled corticosteroids were evaluated by measuring morning cortisol concentration in 49 children taking budesonide and 28 children taking beclomethasone dipropionate. It was found that adrenal suppression occurs in some children given inhaled corticosteroids in doses greater than 400 ug/day. This suppression was dose related and was more pronounced with the use of beclomethasone than budesonide (Ninan et al, 1993). In order to attain such high levels of an inhaled corticosteroid, patients would have to take an overdose. The possibility of accidental overdose can be reduced with proper warning in the package insert; intentional overdose is unlikely, since inhaled corticosteroids are not drugs of abuse. Currently, there is no evidence that the incidence or the course of acute viral or bacterial respiratory infections are affected by the use of inhaled corticosteroids in immunocompetent asthmatics; however, this has not been well studied in children,

and is one issue that may warrant further investigation. In our opinion, it is unlikely that routine examinations by a physician for prescription renewals would make a difference.

These facts presented lead us to conclude that removing the requirement for prescription for inhaled corticosteroids may improve the management of chronic bronchial asthma in many children with negligible additional hazard or risk. In addition, we are requesting that cromolyn, a well-tolerated drug used prophylactically in chronic asthma, be considered for OTC availability as well. Mathison et al studied the use of cromolyn sodium in 30 corticosteroid-dependent adults with severe asthma in a double-blind, double-crossover trial with a subsequent open trial for a duration of 6 to 54 weeks. Of the 29 patients completing the trials, 19 had corticosteroid dose reduction while receiving cromolyn in the double-blind trial, and 22 had corticosteroid dose reduction in the open trial. However, only 10 patients had symptomatic improvement of their asthma (1971). Therefore, it can be concluded that cromolyn is effective in the prevention of asthma in some individuals. In 1996, Pedersen et al conducted a double-blind, placebo-controlled study in 62 children investigating whether sodium cromoglycate at 10 mg in conjunction with terbutaline at 0.5 mg three times daily for 12 weeks can be used as an alternative to inhaled corticosteroids in children with mild-to-moderate asthma. The daily steroid dose was reduced by 50 ug/week for 4 weeks from a starting dose of 200 ug. Only one patient withdrew secondary to worsening asthma from the study group vs. eleven from the placebo group. The study group had fewer symptoms, better morning and evening peak flows, and less requirement for additional beta 2 agonist. Sodium cromoglycate plus terbutaline substituted effectively for inhaled steroid therapy in some patients and can, therefore, be used as an alternative to inhaled corticosteroids in the management of chronic asthma in some children.

We believe that these two drug classes can be made OTC with the potential for some asthmatics to receive more continuous therapy than they now receive because of the need for repeated new prescriptions.

The issue of third party payment for these medications when nonprescription is another issue that must also be addressed by society. The medication and the disease treated are unchanged by the removal of the requirement for a prescription to obtain the medication. Therefore, it is only logical that whether or not treatment of asthma with these inhaled medications is covered by third parties should be determined by factors other than whether a prescription drug is switched to OTC. Third party payment

should be based on the disease and the specific treatment, not on the interpretation of whether or not the drug fails to meet the criteria for prescription requirement of section 503(b)(1) of the act (21 USC 535(b)).

Sincerely yours,

Marie-Helene Sajous

Marie-Helene Sajous

Marcus Reid

Marcus M. Reidenberg, MD

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